Factors associated with late presentation for HIV care and treatment progression among adults in rural South Africa.

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Abstract.

Late presentation for treatment has been one of the major factors limiting the effectiveness of antiretroviral therapy in generalized epidemics. In this contribution we use a composite data source comprising data from the Agincourt Health and Demographic Surveillance System (HDSS) and data from the chronic care units of eight health facilities that residents of the Agincourt HDSS use. Record linkage between the two data sources is done at the health facility and in the presence of the patient, which ensures high quality matches and provides an opportunity to seek informed consent from the patient. We use these data to relate individual and household characteristics collected during routine demographic surveillance (household wealth, household composition, marital status, parenthood status, ...) to (i) late presentation as measured by the CD4 cell count at first presentation, and (ii) the progression form first presentation to treatment initiation.

Extended abstract

Introduction

Population-based studies in Southern and Eastern Africa have shown considerable reductions in adult mortality rates since the introduction of antiretroviral therapy (ART) [1-3]. However, mortality rates of adults who are HIVpositive still remain higher than of those who are HIV negative [4]. Relatively low coverage of HIV Testing and Counseling (HTC), late presentation for treatment, and the low retention of patients have all been cited as factors limiting the potential of ART to reduce mortality rates of HIVpositive adults to same levels as those of their HIV negative counterparts [5-8]

Factors found to be associated with late presentation for HIV/AIDS care in a study in Uganda in 2007 include male sex, older age, lower education level, being unemployed, living in a household with others, being unmarried being not pregnant and not having young children [9]. However, these factors may change over time and may be different for different settings in sub-Saharan Africa.

In this study we use individually-linked data from the Agincourt Health and Demographic Surveillance System (AHDSS) in South Africa, and data from the chronic care units of eight health facilities that residents of the AHDSS use to (i) study individual and household level characteristics of late HIV diagnosis, and (ii) the progression form first presentation to treatment initiation. In this extended abstract we only present evidence of the first of these objectives; by the time of the conference, we will present analyses for both outcomes.

Methods

Data sources

Data used for this study comes from two sources. The first data consists of patient identifiers and clinical characteristics at time of first HIV positive diagnosis collected from patients attending the chronic care units of eight health facilities that residents of

the Agincourt HDSS use. The second dataset consists of individual and household characteristics collected from residents of the Agincourt HDSS.

The data from Agincourt HDSS was collected as part of annual updates of vital events and socioeconomic indicators in a predominantly rural population in northeast South Africa [10, 11]. The population is largely Tsonga-speaking and almost a third comprises former Mozambican refugees who arrived in the area in the early to mid-1980s and their descendants. The population has been under surveillance since 1992 and until 2006 it consisted of residents of 21 villages. The study population was extended to residents of 26 villages in 2007 and residents of 5 more villages were added between 2010 and 2012, all in response to an expanding trials and evaluation portfolio. Currently, the study population consists of some 115,000 people.

Data collection at the chronic care units of eight health facilities started in March 2014, and is ongoing. Whenever a new patient presents to the clinic, a data clerk first explains the study objectives and obtains written informed consent to collect medical data and to link that to the AHDSS. The data clerk subsequently collects a set of identifiers that are used to search the AHDSS database using a probabilistic algorithm described in our previous research [12]. Potential matches are reviewed in the presence of the patient to resolve any uncertainty about his or her identity. In addition to identifying of the patient in the AHDSS database, the data clerk extracts information from the medical records, including the date of the first HIV positive diagnosis; the CD4 count at first diagnosis; date of ART initiation, and logs all follow-up visits.

Statistical Analysis

We define late presenters for HIV care and treatment as patients having a CD4 count $<350 \text{ cells}/\mu\text{L}$ at the time of first HIV positive diagnosis. Descriptive statistics (percentages and medians) are used to summarise demographic characteristics and CD4 count at the time of first HIV positive diagnosis based on data collected in the health facilities. Thereafter, logistic regression models are used to identify individual and household factors that are independently associated with late presentation for HIV care and treatment. Factors considered in these analyses include sex, age, calendar

year of first HIV positive diagnosis, ethnicity (South African, Mozambican and other), marital status, education status, number of other adults in patient's household, having given birth in the last 4 years and tertile of patient's household socioeconomic status. These analyses are performed on the health facility and Agincourt HDSS individually-linked data.

All analyses are performed using STATA version 13.1 (Stata Corp., College Station, USA).

Results

The main dataset used in our study consists of clinical records of 3081 adult HIV positive patients who had a first HIV positive diagnosis between 2011 and 2014. The clinical and sociodemographic characteristics of these patients at the time of first HIV positive diagnosis are shown in Table 1. Overall, most patients are female (75.7%), the median age of all patients is 36 years, the median CD4 count at first HIV positive diagnosis for all patients is 232 cells/ μ L and 79% of all patients presented late for HIV care and treatment. Separate analyses for males and females show that at the time of first HIV positive diagnosis the median age is higher in males compared to females and also that females present with high CD4 count compared to males. In addition, while the proportion of late presenters is high for both males and females, it has decreased more among females than males.

In Tables 2 and 3 we show individual and household factors that are independently associated with late presentation for HIV care and treatment in the health facility and Agincourt HDSS individually-linked data of 2107 females (90.4% of all female patients with clinical records) and 655 males (87.3% of all male patients with clinical records). In multivariable models, factors that are independently associated with late presentation for HIV care and treatment are calendar year of first HIV positive diagnosis (diagnosed in 2011) and tertile of household socioeconomic status (low tertile) in males and calendar year of first HIV positive diagnosis (diagnosed in 2011), age (50 years and older) and having given birth in the last 4 years for females.

Discussion

We have used health facility and demographic surveillance individually-linked data to relate individual and household characteristics collected during routine demographic surveillance (household wealth, household composition, marital status, parenthood status, ...) to (i) late presentation for HIV care and treatment as measured by the CD4 cell count at first presentation. Our analysis shows that although the prortion of late presenters is declining, more than two thirds of females and four fifths of males who are HIV positive present for care and treatment for the first time with CD4 cell counts of <350 cells/ μ L. Of the individual and household factors examined, late presentation for HIV care and treatment is independently associated with low household socioeconomic status in males and old age and not having given birth in the last 4 years in females. The low proportion of late presenters among females compared to males could mainly be attributed to the fact that the former typically have more contact with the healthcare system and are therefore likely to have access to earlier HIV testing and enrollment in HIV care. The same argument also applies to females who gave birth in the immediate past compared to those who did not give birth. The differences in the proportion of late presenters among young compared to older females could also be attributed to the differences in the frequency of contacts with the healthcare system between them. More young than old females have contacts with the healthcare system for antenatal care purposes. The low odds of presenting late in males from households of high compared to those from households of low socioeconomic status could be attributed to the fact that those from high socioeconomic status have better access to resources including knowledge, money, power, prestige, and beneficial social connections that allow them to access medical facilities and services [13-16] including those for HIV testing and care.

Based on these preliminary findings, we argue that the risk of late presentation for HIV care and treatment could be significantly reduced by devising strategies and approaches that would increase contact with the healthcare system for all segments of the population. By the time of the conference, we will include data up to June 2015, refine our statistical models, test other covariates (e.g., parenthood status for men, other adults receiving HIV care in the household, ...) and use other thresholds for the outcome variable (e.g., CD4 <200). In addition, we will present results of the progression from the first presentation for a CD4 cell count to ART ignition. This analysis will be done using competing risks survival analysis as patients may die (the competing event) before initiating treatment (the event of interest).

References

- Herbst AJ, Cooke GS, Bärnighausen T, KanyKany A, Tanser F, Newell ML. Adult mortality and antiretroviral treatment roll-out in rural KwaZulu-Natal, South Africa. Bulletin of the World Health Organization. 2009;87(10):754-62.
- 2. Jahn A, Floyd S, Crampin AC, Mwaungulu F, Mvula H, Munthali F, et al. Population-level effect of HIV on adult mortality and early evidence of reversal after introduction of antiretroviral therapy in Malawi. The Lancet. 2008;371(9624):1603-11.
- 3. Floyd S, Marston M, Baisley K, Wringe A, Herbst K, Chihana M, et al. The effect of antiretroviral therapy provision on all-cause, AIDS and non-AIDS mortality at the population level--a comparative analysis of data from four settings in Southern and East Africa. Tropical Medicine & International Health. 2012;17(8):e84--e93.
- 4. Reniers G, Slaymaker E, Nakiyingi-Miiro J, Nyamukapa C, Crampin AC, Herbst K, et al. Mortality trends in the era of antiretroviral therapy: evidence from the Network for Analysing Longitudinal Population based HIV/AIDS data on Africa (ALPHA). AIDS. 2014 Nov;28 Suppl 4:S533-42. PubMed PMID: 25406756. Pubmed Central PMCID: 4251911.
- 5. Rosen S, Fox MP. Retention in HIV care between testing and treatment in sub-Saharan Africa: a systematic review. PLoS Med. 2011 Jul;8(7):e1001056. PubMed PMID: 21811403. Epub 2011/08/04. eng.
- 6. Rosen S, Fox MP, Gill CJ. Patient retention in antiretroviral therapy programs in sub-Saharan Africa: a systematic review. PLoS Med. 2007 Oct 16;4(10):e298. PubMed PMID: 17941716. Pubmed Central PMCID: 2020494.
- Lawn SD, Harries AD, Anglaret X, Myer L, Wood R. Early mortality among adults accessing antiretroviral treatment programmes in sub-Saharan Africa. AIDS. 2008 Oct 1;22(15):1897-908. PubMed PMID: 18784453. Pubmed Central PMCID: 3816249.
- 8. Staveteig S, Wang S, Head S, Bradley S, Nybro E. Demographic Patterns of HIV Testing Uptake in Sub-Saharan Africa. DHS Comparative Reports No. 30. Calverton, Maryland, USA: ICF International. 2013.

- 9. Kigozi IM, Dobkin LM, Martin JN, Geng EH, Muyindike W, Emenyonu NI, et al. Late disease stage at presentation to an HIV clinic in the era of free antiretroviral therapy in sub-Saharan Africa. Journal of acquired immune deficiency syndromes (1999). 2009;52(2):280.
- 10. Kahn K, Collinson MA, Gómez-Olivé FX, Mokoena O, Twine R, Mee P, et al. Profile: Agincourt Health and Socio-demographic Surveillance System. International Journal of Epidemiology. 2012;41(4):988-1001.
- 11. Kahn K, Tollman SM, Collinson MA, Clark SJ, Twine R, Clark BD, et al. Research into health, population and social transitions in rural South Africa: Data and methods of the Agincourt Health and Demographic Surveillance System. Scandinavian Journal of Public Health. 2007;35(69 suppl):8-20.
- 12. Kabudula CW, Clark BD, Gómez-Olivé FX, Tollman S, Menken J, Reniers G. The promise of record linkage for assessing the uptake of health services in resource constrained settings: a pilot study from South Africa. BMC Medical Research Methodology. 2014;14(1):71.
- 13. Link BG, Phelan J. Social conditions as fundamental causes of disease. Journal of Health & Social Policy. 1995:80-94.
- 14. Link BG, Phelan JC. Fundamental sources of health inequalities. Policy Challenges in Modern Health Care. 2005:71-84.
- 15. Link BG, Phelan JC, Miech R, Westin EL. The resources that matter: fundamental social causes of health disparities and the challenge of intelligence. Journal of Health and Social Behavior. 2008;49(1):72-91.
- 16. Phelan JC, Link BG, Tehranifar P. Social Conditions as Fundamental Causes of Health Inequalities Theory, Evidence, and Policy Implications. Journal of Health and Social Behavior. 2010;51(1 suppl):S28-S40.

	Characteristic					
		2011	2012	2013	2014	Total
	No. of patients	683	777	721	900	3081
	Sex					
	Female	524 (76.72)	576 (74.13)	538 (74.62)	693 (77.00)	2331 (75.66)
	Male	159 (23.28)	201 (25.87)	183 (25.38)	207 (23.00)	750 (24.34)
	Age					
	Median (IQR)	37 (31-47)	36 (29-47)	35 (28-45)	34 (28-44)	36 (29-46)
ed	18-34	278 (40.70)	347 (44.72)	347 (48.40)	454 (50.73)	1,426 (46.43)
bin	35-49	267 (39.09)	271 (34.92)	247 (34.45)	287 (32.07)	1,072 (34.91)
om	50+	138 (20.20)	158 (20.36)	123 (17.15)	154 (17.21)	573 (18.66)
s c	CD4 cell count					
nale	Median CD4 cell count (IQR)	192 (109-280)	240 (150-327)	258 (145-358)	249 (128-377)	232 (134-334)
fem	<200	369 (54.03)	305 (39.20)	263 (36.38)	344 (38.22)	1,281 (41.54)
nd	200-349	260 (38.07)	332 (42.67)	268 (37.07)	298 (33.11)	1,158 (37.55)
s ai	350-499	36 (5.27)	85 (10.93)	92 (12.72)	131 (14.56)	344 (11.15)
lale	500+	18 (2.64)	56 (7.20)	100 (13.83)	127 (14.11)	301 (9.76)
Z	Late presenters	629 (92.09)	637 (81.88)	531 (73.44)	642 (71.33)	2,439 (79.09)
	No. of patients	524	576	538	693	2331
	Age					
lly	Median (IQR)	36 (30-46)	35 (28-45)	33 (27-41)	32 (27-32)	34 (28-43)
on	18-34	240 (45.80)	281 (48.95)	305 (57.22)	396 (57.56)	1,222 (52.70)
ales	35-49	196 (37.40)	187 (32.58)	155 (29.08)	193 (28.05)	731 (31.52)
3m2	50+	88 (16.79)	106 (18.47)	73 (13.70)	99 (14.39)	366 (15.78)
Fe	CD4 cell count					

Table 1. Demographic and clinical characteristics at time of first HIV positive diagnosis of patients attending 8 clinical centres of Agincourt HDSS, South Africa: 2011 to 2014.

	Median CD4 cell count (IQR)	198 (125-284)	252 (163-332)	278 (165-394)	275 (165-400)	248(149-344)
	<200	267 (50.95)	199 (34.55)	174 (32.34)	227 (32.76)	867 (37.19)
	200-349	214 (40.84)	269 (46.70)	201 (37.36)	244 (35.21)	928 (39.81)
	350-499	28 (5.34)	66 (11.46)	76 (14.13)	111 (16.02)	281 (12.05)
	500+	15 (2.86)	42 (7.29)	87 (16.17)	111 (16.02)	255 (10.94)
	Late presenters	481 (91.79)	468 (81.25)	375 (69.70)	471 (67.97)	1,795 (77.01)
	No of patients	159	201	183	207	750
	Age					
	Median (IQR)	41 (35-53)	40 (32-50)	42 (35-51)	41 (34-41)	41 (34-51)
	18-34	38 (23.90)	65 (32.34)	42 (22.95)	58 (28.02)	203 (27.07)
	35-49	71 (44.65)	84 (41.79)	91 (49.73)	94 (45.41)	340 (45.33)
	50+	50 (31.45)	52 (25.87)	50 (27.32)	55 (26.57)	207 (27.60)
	CD4 cell count					
	Median CD4 cell count (IQR)	159 (76-242)	192 (117-297)	207 (121-301)	159 (64-285)	182 (93-286)
	<200	102 (64.15)	106 (52.74)	88 (48.09)	117 (56.52)	413 (55.07)
nly	200-349	46 (28.93)	63 (31.34)	67 (36.61)	54 (26.09)	230 (30.67)
S 0)	350-499	8 (5.03)	19 (9.45)	16 (8.74)	20 (9.66)	63 (8.40)
ale	500+	3 (1.89)	13 (6.47)	12 (6.56)	16 (7.73)	44 (5.87)
M	Late presenters	148 (93.08)	169 (84.08)	155 (84.70)	171 (82.61)	643 (85.73)

NOTE. Data are no. (%) of patients, unless otherwise indicated. IQR = interquartile range.

11255, 50411 111104. 2011 10	Total	Late presenters	Unadjusted OR		Adjusted OR	
	(Number matched $= 2107$)	(row %)	(95% CI)	p-value	(95% CI)	p-value
Year of HIV diagnosis						
2011	484	443 (91.53)	1	-	1	-
2012	530	434 (81.89)	0.41 (0.28-0.61)	0.000	0.43 (0.27-0.68)	0.000
2013	480	342 (71.25)	0.22 (0.15-0.33)	0.000	0.19 (0.12-0.30)	0.000
2014	613	425 (69.33)	0.20 (0.14-0.30)	0.000	0.21 (0.14-0.33)	0.000
Age at time of HIV diagnosis	3					
18-34	1110	832 (74.95)	1	-	1	-
35-49	661	532 (80.48)	1.37 (1.08-1.74)	0.008	1.27 (0.93-1.74)	0.119
50+	332	279 (84.04)	1.75 (1.27-2.43)	0.001	1.87 (1.14-3.09)	0.013
Ethnicity						
Other	664	509 (76.66)	1	-	1	-
South Africa	1443	1135 (78.66)	1.12 (0.90-1.39)	0.303	0.88 (0.66-1.17)	0.396
Has < 5 year old child						
No	1420	1139 (80.21)	1	-	1	-
Yes	687	505 (73.51)	0.68 (0.55-0.84)	0.001	0.75 (0.57-0.99)	0.048
No. of 18+ year old adults in household						
0	360	296 (82.22)	1	-	1	-
1-2	803	611 (76.09)	0.68 (0.50-0.94)	0.02	0.90 (0.57-1.40)	0.642
3-5	706	553 (78.33)	0.78 (0.56-1.08)	0.136	0.98 (0.62-1.53)	0.937
6+	204	158 (77.45)	0.74 (0.48-1.13)	0.17	0.87 (0.50-1.51)	0.628
Marital status						
Single	783	604 (77.14)	1	-	1	-
Cohabiting	270	206 (76.3)	0.95 (0.68-1.32)	0.777	1.18 (0.82-1.69)	0.365

Table 2. Associations between individual and household characteristics with late presentation for HIV diagnosis among females of Agincourt HDSS, South Africa: 2011 to 2014

	Married	272	213 (78.31)	1.06 (0.76-1.49)	0.691	0.98 (0.67-1.43)	0.953
	Separated/divoced	207	159 (76.81)	0.98 (0.68-1.41)	0.921	0.82 (0.55-1.23)	0.354
	Widowed	189	158 (83.6)	1.51 (0.99-2.29)	0.054	1.00 (0.61-1.62)	0.996
Educa	ation status						
	None	202	168 (83.17)	1	-	1	-
	Incomplete primary	261	207 (79.31)	0.77 (0.48-1.24)	0.295	0.94 (0.54-1.65)	0.842
	Complete primary	125	92 (73.6)	0.56 (0.32-0.97)	0.039	0.75 (0.39-1.44)	0.394
	Incomplete						
	Secondary	813	614 (75.52)	0.62 (0.41-0.93)	0.022	1.16 (0.67-2.00)	0.579
	Complete Secondary	517	402 (77.76)	0.70 (0.46-1.07)	0.109	1.26 (0.70-2.25)	0.433
Tertil	es of household socioeconomic status						
	Low	741	563 (75.98)	1	-	1	-
	Middle	658	515 (78.27)	1.13 (0.88-1.46)	0.310	1.09 (0.81-1.47)	0.547
	High	505	398 (78.81)	1.17 (0.89-1.54)	0.243	1.11 (0.79-1.57)	0.518

NOTE. Calculation for different variables may be based on different numbers of patients because of missing data.

11255, 504017 http:// 2011 to 2	Total	Late presenters	Unadjusted OR		Adjusted OR	
	(Number matched $= 655$)	(row %)	(95% CI)	p-value	(95% CI)	p-value
Year of HIV diagnosis						
2011	143	133 (93.01)	1	-	1	-
2012	175	148 (84.57)	0.41 (0.19-0.88)	0.023	0.31 (0.11-0.83)	0.02
2013	165	140 (84.85)	0.42 (0.19-0.91)	0.028	0.34 (0.12-0.90)	0.032
2014	172	144 (83.72)	0.38 (0.18-0.82)	0.014	0.21 (0.07-0.56)	0.002
Age						
18-34	173	144 (83.24)	1	-	1	-
35-49	298	265 (88.93)	1.61 (0.94-2.77)	0.08	1.68 (0.84-3.33)	0.136
50+	184	156 (84.78)	1.12 (0.63-1.97)	0.69	1.84 (0.78-4.29)	0.157
Ethnicity						
Other	207	182 (87.92)	1	-	1	-
South Africa	448	383 (85.49)	0.80 (0.49-1.32)	0.401	0.72 (0.37-1.43)	0.359
No. of 18+ year old adults in h	ousehold					
0	156	137 (87.82)	1	-	1	-
1-2	246	214 (86.99)	0.92 (0.50-1.70)	0.808	0.89 (0.38-2.10)	0.797
3-5	182	150 (82.42)	0.65 (0.35-1.20)	0.169	0.69 (0.29-1.64)	0.407
6+	57	50 (87.72)	0.99 (0.39-2.49)	0.984	1.24 (0.38-4.02)	0.713
Marital status						
Single	169	144 (85.21)	1	-	1	-
Cohabiting	138	123 (89.13)	1.42 (0.71-2.82)	0.311	1.05 (0.49-2.25)	0.899
Married	157	133 (84.71)	0.96 (0.52-1.76)	0.901	0.85 (0.40-1.80)	0.675
Separated/divoced	79	70 (88.61)	1.35 (0.59-3.04)	0.469	1.09 (0.45-2.62)	0.846
Widowed	14	12 (85.71)	1.04 (0.21-4.93)	0.959	0.74 (0.13-4.03)	0.729

Table 3. Associations between individual and household characteristics with late presentation for HIV diagnosis among males of Agincourt HDSS, South Africa: 2011 to 2014

Education status					
None	58	51 (87.93)	1	1	
Incomplete primary	127	105 (82.68)	0.65 (0.26-1.63) 0	.364 0.64 (0.19-2.14) 0.473	
Complete primary	42	37 (88.10)	1.01 (0.29-3.45) 0	.98 0.62 (0.14-2.73) 0.528	
Incomplete Secondary	217	186 (85.71)	0.82 (0.34-1.97) 0	.664 0.94 (0.27-3.26) 0.93	
Complete Secondary	161	140 (86.96)	0.91 (0.36-2.28) 0	.849 1.47 (0.39-5.52) 0.569	
Tertiles of household socioeconomic status					
Low	214	194 (90.65)	1	1	
Middle	190	162 (85.26)	0.59 (0.32-1.09) 0	0.097 0.45 (0.22-0.92) 0.03	
High	178	148 (83.15)	0.50 (0.27-0.93) 0	0.028 0.41 (0.19-0.88) 0.023	

NOTE. Calculation for different variables may be based on different numbers of patients because of missing data